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(54) Title: PROCESS FOR PREPARATION OF (+)-P-MENTHA-2,8-DIENE-1-OL

(57) Abstract: A process for preparing (+)-p-mentha-2,8-diene-1-ol comprising reacting (+)-limonene oxide with at least one amine in the presence of at least one Lewis acid to form amine adduct intermediates. The amine adduct is then oxidized to form an N-oxide that is pyrolyzed to form (+)-p-mentha-2,8-diene-1-ol.

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/IL2004/011509

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C29/10 C07C29/74

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STEINER D ET AL: "A facile and efficient method for the kinetic separation of commercially available cis- and trans-limonene epoxide" TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 13, no. 21, 31 October 2002 (2002-10-31), pages 2359-2363, XP004392003 ISSN: 0957-4166 the whole document	1,2
X	NEWHALL, W. F.: "Derivatives of (+)-Limonene. II. 2-Amino-1-p-menthanols." J. ORG. CHEM., vol. 24, 1959, pages 1673-1676, XP002297508 the whole document	1,2

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
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- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/011509

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ASAO N ET AL: "sigma-pi Chelation-controlled chemoselective ring openings of epoxides" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 42, no. 44, 29 October 2001 (2001-10-29), pages 7903-7905, XP004308032 ISSN: 0040-4039 the whole document</p>	1,2
X	<p>----- NAKAI K ET AL: "A One-pot Aza-Payne Rearrangement-Epoxyde Ring Opening Reaction of 2-Aziridinemethanols: A Regio- and Stereoselective Synthetic Route to Diastereomerically Pure 1,2-Amino Alcohols" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 36, no. 35, 28 August 1995 (1995-08-28), pages 6247-6250, XP004027360 ISSN: 0040-4039 the whole document</p>	1,2
X	<p>----- SMITH, W. B.: "Ring Opening of Epoxides with Morpholine-Borane" J. ORG. CHEM., vol. 49, 1984, pages 3219-3220, XP002297573 the whole document</p>	1,2
X	<p>----- HUDRLIK, P.; HUDRLIK, A.; KULKARNI, A.: "Stereospecific synthesis of enamines from alpha,beta-epoxysilanes" TETRAHEDRON LETT., vol. 26, no. 2, 1985, XP002297753 the whole document</p>	1
X	<p>----- DATABASE BEILSTEIN [Online] BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002297890 retrieved from XFIRE accession no. RID1459337 abstract & EGUCHI, Y.; SASAKI, F.; TAKASHIMA, Y. ET AL.: CHEM. PHARM. BULL., vol. 39, no. 3, 1991, pages 795-797, ----- -/--</p>	1,2

INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BEILSTEIN [Online] BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002297891 retrieved from XFIRE accession no. RID1454331 abstract & GALVEZ, C. AND VILADOMS, P.: HETEROCYCL. CHEM., vol. 21, 1984, pages 421-423, -----</p>	1,2

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US2004/011509

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 2

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,2

Process for the regio- and stereoselective opening of an epoxide ring comprising reacting a compound having an epoxide ring with at least one amine in the presence of at least one Lewis acid.

2. claims: 3-22

Process for preparing (+)-p-mentha-2,8-diene-1-ol analogs from limonene oxide derivatives by treatment with an amine in the presence of a Lewis acid.

3. claim: 23

Method for the diastereomeric separation of a mixture of (+)-cis-limonene oxide and (+)-trans-limonene oxide, the method comprising reacting the mixture with an amine in the presence of a Lewis acid and recovering the (+)-cis-limonene oxide that does not react with the amine.
